REMARKS

The aforementioned amendments to claims 6, 11, 14, and 15, and the addition of new claim 16, are respectfully submitted in response to the official action dated January 9, 2008. In light of these amendments and the remarks which follow, it is respectfully submitted that all of the claims in this application now clearly define patentable subject matter and overcome the rejections set forth in the latest official action herein. Therefore, reconsideration and allowance of these claims is respectfully solicited.

Claim 16 corresponds to claim 1, except that it requires that the active ingredient be present in at least 0.26% by weight of the composition. This limitation is supported in the specification at page 5, paragraph [0023] and page 7, paragraph [0030]. The amendments to claims 6, 11, 14, and 15 are made in response to specific objections raised by the Examiner, and are clearly supported throughout the present specification, or merely include deletions from these claims which are thus also clearly supported therein. No new matter is included in these amendments, and their entry is therefore respectfully solicited.

Claims 11-15 have been rejected as being unpatentable under 35 U.S.C. § 112, first paragraph. The Examiner contends that these claims contain subject matter not described in the specification as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. In particular, the specification is said not to support a particulate carrier with mean particle sizes ranging from about 89 to about 110 in diameter. The limitation in claim 11, however, has now been amended to read from 89 to about 110 microns in diameter, as specifically set forth in Example 1 beginning on page 9 of the specification. Thus, although this example is directed to a specific embodiment of the present

invention, use of the particular range of particle sizes for the particular particulate carrier (namely, lactose) used therein does not alter the fact that this disclosure certainly does reasonably convey to one skilled in the art that applicant had possession of this invention as applied to the subject matter of claim 11. The Examiner goes on to state that the specification only has written support for a dry powder inhalation composition according to claim 9 in which the MDPI is capable of producing 12 mcg dose having an FPF of 49-54% or a 6 mcg dose having an FPF of 48% and not "about" these numbers. However, having amended claims 14 and 15 to delete the term "about," this objection has certainly now been obviated. Furthermore, claims 14 and 15 have also been amended to specifically relate to formoterol, therefore clearly obviating this objection.

Claims 6 and 11 have been rejected as being unpatentable under 35 U.S.C. § 112, second paragraph. The Examiner objects to the recitation of a derivative of formoterol in claim 6. However, in view of the deletion of this limitation from that claim, this objection has now been obviated. Claim 11 is said to be vague because there are no units in the measurement. However, the amendment of claim 11 to include the limitation to the units of microns clearly obviates this objection.

Claims 1, 2, and 5-10 have been rejected as being anticipated by Haeberlin under 35 U.S.C. § 102(b). The Examiner contends that Haeberlin discloses dry powder formulations effective for treating COPD by inhalation as a dry powder comprising formoterol mixed with a diluent or carrier in an amount of 400 to 5,000 micrograms per microgram of formoterol active, and that a composition comprising 400 mcg of diluent and 1 mcg of formoterol active comprises 0.25% w/w active. The mean particle diameter of formoterol active is said to preferably be up to 10 microns, and the diluent or carrier is said to have a

maximum diameter of 300 microns, preferably of 212 microns. In a preferred embodiment, the dry powder is said to be in a capsule where the amount of diluent/carrier is preferably such that the total weight of the dry powder per capsule is between 5 and 25 mg, and the doses of formoterol active are said to be from 1 to 60 mcg. In a preferred embodiment, the dry powder is said to be in a reservoir in a multidose dry powder inhaler adapted to deliver a unit dose. Example 6 is said to disclose a composition where the formoterol active is present in an amount of 0.24% w/w.

In response to applicant's prior arguments, the Examiner has disagreed with applicant's assertions that the amount of active disclosed by Haeberlin does not touch applicant's claimed range because it is 0.249% as opposed to the claimed minimum of 0.25%, stating that when fairly comparing calculated numerical values it is imperative that one utilize the same number of significant figures. Since applicant's claimed minimum is only recited to two significant figures, it is said to be inappropriate to calculate a figure for the prior art using three significant figures. Limiting applicant's calculation to two significant figures, the ranges are said to touch. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

It is first noted that the Examiner's position that analysis of the prior art requires that numerical values be fairly calculated using the same number of significant figures is not supported by the facts or the law, and is deemed to be entirely inappropriate. The question is whether or not the reference anticipates the claimed invention. It clearly does not. Haeberlin does not specifically teach or even suggest any composition with an active containing at least 0.25% active therein. The closest teaching in Haeberlin requires 400 mcg of

diluent for each 1 mcg of active, which can be directly calculated to provide a result of 0.249%. Applicant strongly objects to the exercise of rounding off a figure in the art to somehow assert that it then "teaches" a formulation containing at least 0.25% active. The fact is that this reference does not teach a single point within the claimed range, and therefore an anticipation rejection cannot be based solely upon the Examiner's mathematical exercise.

It is also clear that the Examiner's attempt to stretch the Haeberlin reference to somehow anticipate these claims is not legally appropriate. In *Atofina v. Great Lakes Chem. Corp*,, 441 F.3d 991 (Fed. Cir. 2006), the Federal Circuit reversed a similar attempt to create an anticipatory reference. In *Atofina* the district court had found anticipation of (1) a claimed temperature range of 330°C to 450°C in a reference disclosing a corresponding temperature range of 100°C to 500°C, and a preferred temperature range of 150°C to 350°C; and (2) a claimed oxygen to methylene molar ratio of 0.1% to 5.0% in a reference disclosing a corresponding oxygen to methylene molar ratio of 0.001 to 1.0%. In reversing, the Federal Circuit stated that "[g]iven the considerable difference between the claimed range and the range in the prior art, no reasonable fact finder could conclude that the prior art describes the claimed range with sufficient specificity to anticipate this limitation of the claim." (*Id.* at 999.) The court went on to analyze the contention that the reference anticipated the temperature range because the preferred range slightly overlapped the claimed range. Here the court stated:

> But that slightly overlapping range is not disclosed as such, *i.e.*, as a species of the claimed generic range of 330 to 450°C. Moreover, the disclosure of a range of 150 to 350°C does not constitute a specific disclosure of the endpoints of that range, i.e., 150°C to 350°C . . . . The disclosure is only that of a range, not a specific temperature in that range, and

> the disclosure of a range is no more a disclosure of the end points of the range than it is of each of the intermediate points. This [the reference] does not disclose a specific embodiment of the claimed temperature range

Id. at 1000.

A similar conclusion was reached with respect to the oxygen to methylene molar ratios. In all respects, Haeberlin clearly does not anticipate the claims pending in this application, and withdrawal of this rejection is therefore respectfully solicited. Furthermore, with respect to new claim 16, it is certainly clear that this claim does not overlap with the disclosure in Haeberlin. Indeed, since the Examiner has not rejected claims such as claim 3 on the basis of Haeberlin in this rejection, it is clear that this rejection is no longer applicable to claim 16.

The Examiner has next referred to this application as naming joint inventors, with reference to Rule 56 therein. It is pointed out, however, that there is a sole inventor listed in this application.

Claims 1-6 and 8-15 have been rejected as being unpatentable over Haeberlin under 35 U.S.C. § 103(a). The Examiner admits that Haeberlin does not teach dry powder compositions comprising about 0.26% w/w to about 1% w/w of active ingredient. The Examiner concludes, however, that it would be obvious to optimize the amounts of formoterol in the Haeberlin composition based on the needs of subjects in need of formoterol. While the ratios described in Haeberlin are said to be particularly effective formulations for treating COPD, the description as being "particularly effective" is said not to constitute a teaching away from compositions with greater amounts of formoterol active relative to the diluent/carrier. Optimization is said to be routine practice and obvious to one of ordinary skill in the art. In response to applicant's

arguments, the Examiner further contends that it would have been well within the capacity of the ordinary skilled artisan to adjust the amount of active agent in a dry powder formulation for the needs of subjects in need of treatment. Furthermore, modification of the amount of active is said to be an obvious way to increase the active administered to a subject, as well as modifying the amount of a given active agent administered. No particular criticality regarding the amount of active present is said to have been demonstrated nor that amounts greater than 0.25% w/w yield unexpected or surprisingly results or that amounts below 0.25% w/w exhibit undesirable properties. As for the FPF fractions in claims 14 and 15, after admitting that Haeberlin is silent, the Examiner reminds applicant that the office lacks laboratory facilities to test the compositions of Haeberlin to determine the FPF that these would exhibit on administration. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

It being admitted that the Haeberlin reference does not teach the specific formulation and amounts of active set forth in the claims, the issue is whether a *prima facie* case of obviousness has been made out. To merely state that, in effect, any such formulation would be obvious to one of skill in the art is not believed to meet this burden. Most particularly, as described in the specification in connection with these types of TPI devices, the drug particles are blended with an excipient to create a generally homogeneous mixture. The larger particle size of the excipient results in the powder mixture being flowable and the homogeneity of the mixture enables it to be metered into accurately measurable dosages. This is said to be of particular importance when only very small quantities of drug are required in a dose. With the use of greater percentages of active ingredient than those disclosed in the prior art,

applicant has demonstrated in the examples that he was able to achieve excellent dose uniformity irrespective of this fact. This, of course, is a critical factor in connection with such multidose inhalers and is not suggested by the Haeberlin reference. In Example 2, the results demonstrate an extremely efficient and reproducible blending and handling process with compositions giving excellent dose uniformity. There is also no difference in the fine particle fraction of formoterol between the 6 mcg and 12 mcg strength products, indicating consistent performance of these products. None of this is suggested in the Haeberlin reference. Therefore, the blanket statement that one of ordinary skill in this art would be able to place any amount of active in the composition and expect to get results, particularly in the face of a reference which not only fails to teach the amounts of active required by the present claims, but specifically states that the amounts set forth in Haeberlin were "particularly effective," cannot in applicant's view be taken as a teaching or suggestion to utilize the far different amounts claimed herein. As applicant has also previously asserted, persons skilled in this art would not have further "optimized" the amount of formoterol to produce a composition in which that amount is outside the range disclosed by Haeberlin. Furthermore, "[a] particular parameter must first be recognized as a result-effective variable, *i.e.*, a variable which achieves a recognized result, before the determination of the optimum or workable range of said variable might be characterized as routine experimentation." M.P.E.P. (8th ed, Rev. 5, August 2006), at 2100-71 (citing *In re Antonie*, 559 F.2d 618, 195 U.S.P.Q. 6 (C.C.P.A. 1977)).

Applicant has convincingly demonstrated that the presently claimed dry powder formulations are more accurately metered and provide more uniform and consistent dispersions when dispensed by MDPI devices. Such dry powder formulations would

not have been produced by optimization based on patient needs. Patient needs determine the amounts of drug delivered to a patient which may be varied by varying the quantity of the dry powder formulation delivered without varying the proportion of the drug in the formulation as in accordance with the present invention.

It is therefore respectfully submitted that all of the claims in this application now possess the requisite novelty, utility of unobviousness to warrant their immediate allowance, and such action is therefore respectfully solicited.

Claims 1, 4-7, and 9 have been rejected on the basis of obviousness-type double patenting over claims 1 and 9-11 of co-pending Application No. 10/646,361 in view of Haeberlin. Applicant again respectfully requests, however, that this obviousness-type double-patenting rejection be held in abeyance until the prosecution of this application has been completed.

Applicant again respectfully requests that the Examiner reconsider these rejections and allow the present claims in their present form. If, however, for any reason the Examiner does not believe that such action can be taken, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,

By _____

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